LHCGR gene

luteinizing hormone/choriogonadotropin receptor

Normal Function

The *LHCGR* gene provides instructions for making a receptor protein called the luteinizing hormone/chorionic gonadotropin receptor. Receptor proteins have specific sites into which certain other proteins, called ligands, fit like keys into locks. Together, ligands and their receptors trigger signals that affect cell development and function.

The protein produced from the *LHCGR* gene acts as a receptor for two ligands: luteinizing hormone and a similar hormone called chorionic gonadotropin. The receptor allows the body to respond appropriately to these hormones. In males, chorionic gonadotropin stimulates the development of cells in the testes called Leydig cells, and luteinizing hormone triggers these cells to produce androgens. Androgens, including testosterone, are the hormones that control male sexual development and reproduction. In females, luteinizing hormone triggers the release of egg cells from the ovaries (ovulation); chorionic gonadotropin is produced during pregnancy and helps maintain conditions necessary for the pregnancy to continue.

Health Conditions Related to Genetic Changes

familial male-limited precocious puberty

At least 17 *LHCGR* gene mutations have been identified in boys and men with familial male-limited precocious puberty. These mutations replace single protein building blocks (amino acids) in the luteinizing hormone/chorionic gonadotropin receptor. The mutations cause the receptor to be constantly turned on (constitutively activated), even when not attached (bound) to luteinizing hormone or chorionic gonadotropin. Researchers suggest that the change in amino acid sequence may lead to constitutive activation by changing the shape or other properties of the receptor.

In males, the overactive receptor causes the Leydig cells to produce an excess of testosterone, leading to familial male-limited precocious puberty. Affected boys begin exhibiting the signs of puberty, such as genital growth and pubic hair, between the ages of 2 and 5. The overactive receptor has no apparent effect on females.

Leydig cell hypoplasia

LHCGR gene mutations that cause Leydig cell hypoplasia disrupt luteinizing hormone/chorionic gonadotropin receptor function, impeding the body's ability to react to these hormones. In males, the mutations result in poorly developed or absent

Leydig cells and impaired production of testosterone. A lack of testosterone interferes with the development of male reproductive organs before birth and the changes that appear at puberty.

Mutations that prevent the production of any functional receptor protein cause more severe signs and symptoms of Leydig cell hypoplasia. Affected individuals with a typical male chromosome pattern (46,XY) have female external genitalia and small testes that are undescended, which means they are abnormally located in the pelvis, abdomen, or groin. Severely affected individuals do not develop secondary sex characteristics, such as increased body hair, at puberty.

LHCGR gene mutations that allow some receptor protein function cause milder signs and symptoms of Leydig cell hypoplasia. Affected males may have a range of genital abnormalities, including a small penis (micropenis), the opening of the urethra on the underside of the penis (hypospadias), or a scrotum divided into two lobes (bifid scrotum). Because of these abnormalities, the external genitalia may not look clearly male or clearly female (ambiguous genitalia).

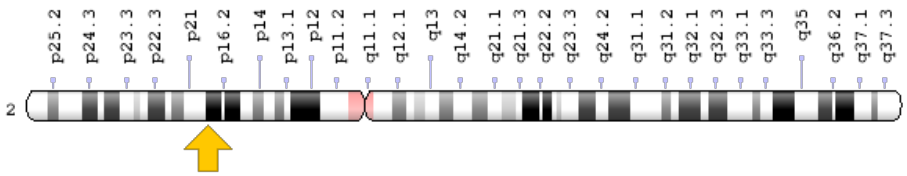
other disorders

Although people who are genetically female (with two X chromosomes in each cell) may inherit mutations in both copies of the *LHCGR* gene that disrupt luteinizing hormone/chorionic gonadotropin receptor function, they do not have Leydig cell hypoplasia because they do not have Leydig cells. Females with the same *LHCGR* gene mutations that cause Leydig cell hypoplasia in males have normal female genitalia and normal breast and pubic hair development, but they may begin menstruation later than usual (after age 16) and have irregular menstrual periods. These mutations also prevent ovulation, leading to an inability to have children (infertility).

Chromosomal Location

Cytogenetic Location: 2p16.3, which is the short (p) arm of chromosome 2 at position 16.3

Molecular Location: base pairs 48,686,774 to 48,755,741 on chromosome 2 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- FLJ41504
- HHG
- LCGR
- LGR2
- LH/CG-R
- LH/CGR
- LHR
- LHRHR
- LSH-R
- LSHR_HUMAN
- luteinizing hormone/choriogonadotropin receptor precursor
- lutropin/choriogonadotropin receptor
- ULG5

Additional Information & Resources

Educational Resources

- Endocrinology (first edition, 2001): Control of Steroid Production in the Fetal Gonads
  https://www.ncbi.nlm.nih.gov/books/NBK29/#A1056

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28LHCGR%5BTIAB%5D%29+OR+%28luteinizing+hormone/choriogonadotropin+receptor%5BTIAB%5D%29%29+OR+%28%28HHG%5BTIAB%5D%29+OR+%28LHR%5BTIAB%5D%29+OR+%28LCGR%5BTIAB%5D%29+OR+%28LGR2%5BTIAB%5D%29+OR+%28LHRHR%5BTIAB%5D%29+OR+%28LH/CGR%5BTIAB%5D%29+OR+%28LH/CG-R%5BTIAB%5D%29+OR+%28lutropin/choriogonadotropin+receptor%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D

OMIM

- LUTEINIZING HORMONE/CHORIOGONADOTROPIN RECEPTOR
  http://omim.org/entry/152790

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/LHRID288.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=LHCGR%5Bgene%5D
- HGNC Gene Family: Glycoprotein hormone receptors
  http://www.genenames.org/cgi-bin/genefamilies/set/199
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=6585
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/3973
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  http://www.uniprot.org/uniprot/P22888

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